



## **OFFICE OF SCIENCE AND TECHNOLOGY POLICY**

### **Request for Information; Potential Changes to the Policies for Oversight of Dual Use Research of Concern (DURC) and the Potential Pandemic Pathogen Care and Oversight (P3CO) Policy Framework**

**AGENCY:** Office of Science and Technology Policy (OSTP).

**ACTION:** Notice of request for information.

**SUMMARY:** Life sciences research is vital for improving health outcomes and protecting the Nation from infectious disease threats, but a small subset of this research could potentially pose risk of accidents or misuse that could harm human health. It is important to regularly evaluate and update biosafety and biosecurity oversight policies to keep pace with new technological developments and the evolving risk landscape. The Office of Science and Technology Policy (OSTP) invites comments on potential changes to the Policies for Federal and Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC) and Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO). These policies establish frameworks for review and oversight requirements for certain categories of life sciences research, namely research with certain pathogens and toxins, including at institutions that accept Federal funding for such research. These requirements are intended to complement activities under existing Federal regulations or guidelines such as the Federal Select Agent Program. OSTP requests comments on how potential changes to these research oversight policies could mitigate risks associated with DURC and research with enhanced potential pandemic pathogens (ePPP) while minimizing undue burden on institutions. The public input provided through this Request for Information (RFI) will inform policy evaluations and issuance of a revised policy (Revised Policy).

**DATES:** Responses are due by 11:59 p.m. Eastern Time on [INSERT DATE 45 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Submissions received after the deadline may not be taken into consideration.

**ADDRESSES:** Comments must be submitted via the Federal eRulemaking Portal at *regulations.gov*. However, if you require an accommodation or cannot otherwise submit your comments via *regulations.gov*, please use the email or phone number listed under “FOR FURTHER INFORMATION CONTACT”. OSTP will not accept comments by fax or by email. To ensure that OSTP does not receive duplicate copies, please submit your comments only once. Additionally, please include the Docket ID (EOP-2023-0001) at the top of your comments.

*Federal eRulemaking Portal:* Go to [www.regulations.gov](http://www.regulations.gov) to submit your comments electronically. Information on how to use *Regulations.gov*, including instructions for accessing agency documents, submitting comments, and viewing the docket, is available on the site under “FAQ” (<https://www.regulations.gov/faq>).

*Privacy Note:* OSTP’s policy is to make all comments received from members of the public available for public viewing in their entirety on the Federal eRulemaking Portal at [www.regulations.gov](http://www.regulations.gov). Therefore, commenters should be careful to include in their comments only information that they wish to make publicly available. OSTP requests that no proprietary information, copyrighted information, or personally identifiable information be submitted in response to this RFI.

*Instructions:* Response to this RFI is voluntary. Each individual or organization is requested to submit only one response. Commenters can respond to one or multiple questions. Submissions are suggested to not exceed the equivalent of ten (10) pages in 12 point or larger font. Submissions should clearly indicate which questions are being addressed. Responses should include the name(s) of the person(s) or organization(s) filing the response. Responses containing references, studies, research, and other

empirical data that are not widely published should include copies of or electronic links to the referenced materials. Responses containing profanity, vulgarity, threats, or other inappropriate language or content will not be considered.

Please note that the U.S. Government will not pay for response preparation, or for the use of any information contained in the response. A response to this RFI will not be viewed as a binding commitment to develop or pursue the project or ideas discussed.

**FOR FURTHER INFORMATION CONTACT:** Direct questions to Asad Ramzanali, [research-oversight-policy@ostp.eop.gov](mailto:research-oversight-policy@ostp.eop.gov), or 202-456-4444.

**SUPPLEMENTARY INFORMATION:** Life sciences research is essential to the scientific advances that underpin improvements in the health and safety of the public, agricultural crops, and other plants, animals, and the environment. While life sciences research provides enormous benefits to society, there can be risks associated with certain subsets of work, typically related to biosafety and biosecurity, that can and should be mitigated. The United States has existing, complementary statutes, regulations, policies, and guidelines that address these potential biosafety and biosecurity risks, particularly those associated with research oversight and management.<sup>1</sup> Together these existing regulatory authorities and guidelines provide a foundation to ensure that scientific research and innovation is safe and secure.

Scientists, institutions, and the USG have gained valuable insight over the past decade from implementing research oversight policies such as the policies for oversight of

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<sup>1</sup> Examples include: Select Agents and Toxins Regulations (42 CFR part 73, 9 CFR part 121, and 7 CFR part 331); National Institutes of Health Guidelines on Research Involving Recombinant and Synthetic Nucleic Acids; ([https://osp.od.nih.gov/wp-content/uploads/NIH\\_Guidelines.pdf](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf)); Biosafety in Microbiological & Biomedical Laboratories (BMBL) 6th Edition (<https://www.cdc.gov/labs/BMBL.html>); Additional U.S. Laws, Regulations and Guidelines (<https://www.phe.gov/s3/law/Pages/default.aspx>)

DURC<sup>2</sup> and the P3CO Policy Framework<sup>3</sup>. During this time, advances in science and technology have occurred that present realized and potential future benefits. However, these advances also present potential risks of misuse. The National Science Advisory Board for Biosecurity (NSABB), a Federal advisory committee that addresses issues related to biosecurity and dual use research, provided recommendations in a March 2023 report<sup>4</sup> to inform United States Government (USG) policy evaluations and the development of a more comprehensive and integrated framework for the oversight of research with pathogens and toxins that may pose significant biosafety or biosecurity risks. Since the release of this report, OSTP has been working with Federal departments and agencies to review, harmonize, and revise these policies in accordance with USG goals of promoting safe and secure biological practices and strengthening responsible conduct for biological research as outlined in the 2022 National Biodefense Strategy and Implementation Plan<sup>5</sup>.

The policy review and revision process has three broad goals:

1. Assess whether and how to merge the existing Federal DURC, Institutional DURC, and P3CO policies into a harmonized policy that addresses oversight for research with pathogens and toxins.
2. Consider revising the scope of the Federal DURC, Institutional DURC, and P3CO policies to include a broader set of pathogens and toxins, including – but not

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<sup>2</sup> United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (<https://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf>); United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (<https://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf>)

<sup>3</sup> Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO) (<https://www.phe.gov/s3/dualuse/Documents/P3CO-FinalGuidanceStatement.pdf>)

<sup>4</sup> Proposed Biosecurity Oversight Framework for the Future of Science (nih.gov); <https://osp.od.nih.gov/wp-content/uploads/2023/03/NSABB-Final-Report-Proposed-Biosecurity-Oversight-Framework-for-the-Future-of-Science.pdf>

<sup>5</sup> National Biodefense Strategy and Implementation Plan: <https://www.whitehouse.gov/wp-content/uploads/2022/10/National-Biodefense-Strategy-and-Implementation-Plan-Final.pdf>

limited to – biological select agents and toxins (BSAT) that impact humans or have the potential to impact humans.

3. Examine ways to strengthen effective implementation of oversight for life sciences research on pathogens and toxins throughout the research lifecycle.

The USG acknowledges that effective oversight helps maintain public trust in the life sciences research enterprise by demonstrating that the scientific community recognizes the implications of research conducted and is acting responsibly to protect public welfare and preserve national security.

*Scope:* OSTP invites comment from any interested stakeholders. In particular, OSTP is interested in input from research institutions, including both domestic and international entities, currently subject to the PC3O Policy or the DURC policies or that may be subject to the revised scope of a potential policy update, researchers within those institutions, scientific and professional organizations, and organizations representing diverse interests across the U.S. research ecosystem.

*Information Requested:* Respondents may provide information for one or more of the topics included below. Respondents are asked to note the corresponding number/s to which responses pertain.

1. The NSABB recommended that USG develop an integrated approach to oversight of research that raises significant biosafety and biosecurity concerns, including ePPP research and DURC (Recommendation 1). By merging the existing Federal DURC, Institutional DURC, and P3CO policies into a harmonized policy, a merged policy could potentially adopt the institutional applicability outlined in the Institutional DURC policy framework, making the following entities subject to a Revised Policy:
  - U.S. Government departments and agencies that fund, sponsor, or conduct life sciences research.

- Institutions within the United States or its territories that both:
    - Receive U.S. Government funds to conduct or sponsor life sciences research; and,
    - Conduct or sponsor research that is within the revised scope, regardless of the source of the funding for the specific project.
  - Institutions outside of the United States that receive U.S. Government funds to conduct or sponsor research that falls under the scope.
    - a) What are the anticipated benefits and challenges of applying a Revised Policy, inclusive of both DURC and ePPP research, to the scope of entities outlined above?
    - b) What are the anticipated benefits and challenges of investigators and institutions having primary responsibility for identification of both DURC and ePPP research?
    - c) What types of resources or tools would be useful for researchers and institutions to determine if their research falls into a revised policy scope that is risk-based rather than list-based, and adequately conduct risk assessments to identify DURC and ePPP research?
2. Currently, the scope of the DURC policies is research that uses one or more of 15 listed agents or toxins and that produces, or is anticipated to produce, any of seven listed experimental effects. The NSABB recommended that the scope of research requiring review for potential DURC should include research that directly involves *any* human, animal, or plant pathogen, toxin, or agent that is reasonably anticipated

to result in one or more of the seven experimental effects outlined in the DURC policy<sup>6</sup> (Recommendation 10.1).

- a. Considering the diversity of federally-funded research settings and portfolios, how would adoption of NSABB's Recommendation 10.1 affect policy implementation and research programs at the institutional level?
- b. Rather than including *any* pathogen within the scope of DURC review, one possible modification of Recommendation 10.1 would be to include DURC experiments that utilize:
  - i. HHS and Overlap Biological Select Agent and Toxins (BSAT) List<sup>7</sup> and/or
  - ii. Pathogen risk group (RG) classification of 3 or 4<sup>8</sup> and/or
  - iii. Any pathogen where the conduct of work (e.g., one of the DURC experimental categories) would require biosafety level 3 or 4 containment.

Would a modification of Recommendation 10.1, in line with the outlined scope of pathogens above, be useful for policy implementation? What specific benefits, challenges, and/or gaps are anticipated by this revised scope?

- c. Are there other risk-based approaches that would expand the scope beyond the current list of 15 agents and toxins provided in the DURC policy that

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<sup>6</sup> United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (<https://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf>); United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (<https://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf>)

<sup>7</sup> Select Agents and Toxins Regulations (42 CFR part 73, 9 CFR part 121, and 7 CFR part 331)

<sup>8</sup> Risk groups as defined in "NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules" ([https://osp.od.nih.gov/wp-content/uploads/2019\\_NIH\\_Guidelines.htm](https://osp.od.nih.gov/wp-content/uploads/2019_NIH_Guidelines.htm))

would facilitate the identification of research that poses significant risks by investigators and institutions while not resulting in undue burdens?

- d. Given the possible revised scope of research requiring review for potential DURC, what modifications, if any, to the current DURC policy list of 7 experimental effects should be considered for a Revised Policy that captures appropriate research without hampering research progress?
- e. What resources or tools would be valuable to assist with implementation of a DURC policy with a scope that is revised to include more than the current list of 15 agents and toxins?

- 3. A PPP is currently defined in the P3CO policy framework<sup>9</sup> as: “a pathogen that satisfies both of the following: 1. It is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations; and 2. It is likely highly virulent and likely to cause significant morbidity and/or mortality in humans.”

The NSABB recommended that the definition of PPP be modified to: (1) Likely moderately or highly transmissible and likely capable of wide and uncontrollable spread in human populations; and/or (2) Likely moderately or highly virulent and likely to cause significant morbidity and/or mortality in humans; and, in addition (3) Likely to pose a severe threat to public health, the capacity of public health systems to function, or national security” (Recommendation 2).

- a) How would the change in the definition of PPP affect the overall scope of a Revised Policy and its subsequent implementation?

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<sup>9</sup> Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO) (<https://www.phe.gov/s3/dualuse/Documents/P3CO-FinalGuidanceStatement.pdf>)



- b) One possible modification to the NSABB PPP definition is to specify a respiratory route of transmission within clause (1). Would that definition of PPP be an appropriate scope to mitigate risks and enhance effective implementation?
  - c) Do you have additional suggestions to modify the PPP definition to mitigate the most significant risks not currently addressed and enhance effective implementation, while limiting negative or unintended consequences and burden on researchers, institutions, and the Federal government?
  - d) Are there characteristics related to human pathology, pathogen characteristics, or other features that would be helpful to clarify the intent of “moderately virulent”? Are there characteristics related to human pathology that would be helpful to clarify the intent of “moderately transmissible”?
4. A Government Accountability Office (GAO) report from January 2023<sup>10</sup> recommended that the Department of Health and Human Services funding agencies should develop and document a standard to define “reasonably anticipated” to ensure consistency in identifying research that falls within scope of a Revised Policy. One possible definition of “reasonably anticipated” is: “‘Reasonably anticipated’ describes an assessment of an outcome that an individual with scientific expertise relevant to the research in question would expect this outcome to occur with a non-trivial likelihood. It does not require high confidence that the outcome will definitely occur and excludes experiments in which an expert would anticipate the outcome to be technically possible, but highly unlikely.”
- a) Does this definition of “reasonably anticipated” provide additional clarity to ensure greater consistency in identifying research that falls within scope of the

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<sup>10</sup> Public Health Preparedness: HHS Could Improve Oversight of Research Involving Enhanced Potential Pandemic Pathogens. (GAO-23-105455)

Revised Policy? What modifications to this definition (if any) would be most helpful?

5. NSABB recommends the removal of blanket exclusions for research activities associated with surveillance and vaccine development or production for research with ePPPs (Recommendation 3).
  - a) Should exemptions for certain activities be included in a Revised Policy?
  - b) What are the benefits and drawbacks of including exemptions for domestic and international pandemic preparedness, biosafety, biosecurity, and global health security?
  - c) If exemptions are included, how could they be bounded to maximize safety and security and minimize negative impact on domestic and global public health including outbreak and pandemic preparedness and response? For example, would vaccine research and development activities be unjustifiably impeded if the current P3CO policy framework exemption for “Activities associated with developing and producing vaccines, such as generation of high growth strains” was either removed completely or modified to “Research on PPPs directly associated with testing and/or producing vaccines, such as generation of high growth strains”?
6. NSABB recommends that continued assessment of the risks and benefits associated with advances and applications of bioinformatics, modeling, and other *in silico* experimental approaches and research involving genes from or encoding pathogens, toxins, or other agents must inform future evaluations of the scope of research oversight policies to help ensure that associated risks are appropriately identified and managed. (Recommendation 10.2). This type of research is not currently included in the DURC and ePPP oversight policies.

- a) Is there a subset of such *in silico* research that should require risk assessment and review in a Revised Policy, and if so, how should this research be defined so that the Policy captures the appropriate research without hampering activities with limited biosecurity risks?
- b) One possible way to define this category of *in silico* research within a Revised Policy would be to include experiments that are reasonably anticipated to:
- “i) Develop *in silico* models that directly enable the predictive design of an enhanced potential pandemic pathogen or novel pathogen or toxin covered under a Revised Policy that could be constructed via genomic editing or *de novo* synthesis; and/or
  - ii) Develop a dataset(s) connecting nucleic acid or amino acid sequences with experimentally-determined pathogenic functions in a manner sufficient to enable the development of *in silico* models described in (i).”

If a new category of research, similar to the examples provided above, were to require risk assessment and review in a Revised Policy, what would be the benefits and challenges with implementation?

Dated: August 28, 2023.

**Stacy Murphy,**

*Deputy Chief Operations Officer/Security Officer.*